REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim Status

Claims 1, 12, and 23-32 are pending, and elected claims 1, 12, 23, 25, and 32 are presented for examination.

Rejections under 35 U.S.C. § 103

Claims 1, 12, 23, and 25 remain rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Treon *et al.*, in view of Ohtomo *et al.*, and Chiriva-Internati *et al.*, further in view of WO 200177362, as evidenced by Porgador *et al.* Office Action, item 4, pages 2-5. Additionally, claims 1, 12, 23, 25, and 32 remain rejected under 35 U.S.C. § 103 (a) as allegedly obvious over Treon *et al.*, in view of Ohtomo *et al.*, and Chiriva-Internati *et al.*, further in view of WO 200177362, as evidenced by Porgador *et al.*, and in further view of Thurner *et al.* *Id.* at item 5, page 5.

While admitting "Chiriva-Internati *et al.* do not teach pulsing dendritic cells directly with HM1.24 antigen, the PTO states that "the state of the prior art is that dendritic cells can be pulsed (loaded) with various agents including whole tumor antigen, naked DNA or whole tumor RNA (see page 604, left column of Treon *et al.*)." *Id.* at page 4. Thus, the PTO alleges "it would have been obvious to one skilled in the art to either pulse dendritic cells via an adeno-associated viral vector/HM1.24 recombinant, or pulse dendritic cells withHM1.24 antigen or peptides thereof." *Id.* at paragraph bridging pages 4-5. Applicants respectfully disagree.

In order to validate a conclusion that a claim would have been obvious, the PTO must demonstrate that one of ordinary skill in the art could have combined the elements in the manner claimed, via known methodology, with no change in the respective function(s) of the elements and with the resultant combination yielding nothing more than predictable results.

KSR v. Teleflex, 127 S. Ct. 1727, 1739 (2007). If any of these requirements does not pertain, then the PTO is barred from concluding that the claim in question would have been obvious.

Such is the case here because before Applicants' discovery, the art was wholly unaware that pulsing a soluble (not full length) HM1.24 protein or peptide results in DC cell stimulation of T cells, which then also react strongly with autologous tumor cells. Thus it was Applicants and not the cited art who pulsed with soluble HM1.24 and made these surprising discoveries, none of which could have been predicted by any combination of the cited art.

As background, generally, when a cancer antigen protein is taken into DC cells, the protein is broken into peptides of about 8-10 amino acid residues, wherein the peptides complex with an MHC Class I molecule, and the complex is presented on the surface of the DC cells. T cells are activated to the CTL, which specifically recognizes the complex and then kills cancer cells expressing the complex. Because the CTL kills only those cancer cells expressing a complex recognized by the CTL, the CTL acts in a complex-specific manner.

Contrary to the present disclosure, Chiriva-Internati describes a viral vector comprising a HM1.24 ***gene***, and not pulsing a dendritic cell with a soluble ***protein/peptide***. Thus, Chiriva-Internati discloses that a strong CTL activity is caused by *expressing* full length HM1.24 in DC cells.

Also, it is not surprising that Chiriva-Internati discloses using a full length HM1.24 because using less than a full length HM1.24 sequence could fail to activate CTL, as a shortened sequence may not contain residues required for activating CTL. For example, HM1.24 residues necessary for activating CTL may be deleted in creating a soluble protein/peptide.

Additionally, while the Office understands that the rationale to modify or combine the prior art may be expressly or impliedly contained in the prior art or reasoned from knowledge available to a skilled artisan, the Office still disregards the MPEP and patent laws, and makes the rejection without consideration of the teachings in the art which discourage the

combination. In fact, it appears that the Office is improperly using hindsight reconstruction to arrive at the presently claimed invention.

For example, Chiriva-Internati teaches that for introduction of a protein into dendritic cells, the protein must be continuously expressed by introducing HM1.24 gene-containing viral vector into dendritic cells because the half life of the protein is very short. Accordingly, Chiriva-Internati, a reference heavily relied upon by the Office in the rejection, destroys the motivation for pulsing a soluble HM1.24 protein/peptide into dendritic cells.

Moreover, the present inventors surprisingly discovered that not only does pulsing with soluble HM1.24 protein result in DC cell stimulation of T cells, but the T cells strongly react with autologous tumor cells. *See* Applicants' specification, e.g., Figure 1, Example 1, and Table 1. Furthermore, Applicants discovered that in 5 MM patients, HM1.24-specific T cells respond to autologous plasma cells. *Id.* at Examples 1 and 2. These unexpected advantages would not have been anticipated by the combination of the cited references.

Furthermore, the Office withdrew the previous obviousness rejection of the claims over Treon, in view of Ohtomo and Chiriva-Internati. Thus, the Office recognized the deficiencies in the teachings of these references. Although the current rejection supplements the primary references with WO 200177362 and Porgador, and optionally Thurner, the addition of a reference which relates to immunoassays (WO 200177362), dendritic cells pulsed with class I restricted peptides (Porgador), and/or dendritic cells pulsed with Mage-3A-1 (Thurner) do not cure these deficiencies either, especially when nothing in the cited art would not lead a skilled artisan to specifically use a soluble HM1.24 protein or peptide to make a cancer vaccine, or recognize the unexpected advantages in doing so.

Thus, the art does not provide the motivation to combine the references and teach each and every element of the presently claimed invention. Therefore, for at least the reasons provided herein, Applicants respectfully request the rejections be withdrawn.

CONCLUSION

Applicants believe that the present application is in condition for allowance.

The Examiner is invited to contact the undersigned if a telephone interview would advance prosecution.

Respectfully submitted,

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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.